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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,783	01/25/2002	Anthony C. Forster	AFOR-P01-001	9343
28120	7590	09/22/2004	EXAMINER	
ROPE & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			KAM, CHIH MIN	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,783	FORSTER ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-11,13-17,19 and 23-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 9 and 10 is/are allowed.
- 6) ☒ Claim(s) 1,4,7,8,11,14,19,23,24,38-41 and 44-51 is/are rejected.
- 7) ☒ Claim(s) 2,5,6,13,15-17,25-37,42 and 43 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/2/04;6/15/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-17 and 19 in the amendment filed June 15, 2004 is acknowledged. The traversal is on the ground(s) that the search can be made without burden for all the claims. This is not found persuasive because applicant's response has not demonstrated there is no search burden. Restriction is proper when two or more claimed inventions are either independent **or** distinct. See MPEP 803. Furthermore, coexamination of each of the additional groups would have required a search of additional classes and art areas. For example, if Groups II and III were included, it would require additional search in class 530, subclass 350, and class 435, subclass 7.1, and the art areas of peptide and drug discovery. Therefore, coexamination of each of these inventions would require a serious additional burden of search.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

2. Claims 1-2, 4-11, 13-17, 19 and 23-51 are pending.

Applicants' amendment filed June 15, 2004 is acknowledged. Applicant's response has been considered. Claims 1-2, 4-11, 13-16 and 19 have been amended, claims 3, 12, 18 and 20-22 have been cancelled, and new claims 23-51 have been added. Therefore, claims 1-2, 4-11, 13-17, 19 and 23-51 are examined.

Information Disclosure Statement (IDS)

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3. The IDS, which was filed March 2, 2004 but was not scanned and considered in the previous Office Action, and supplemental IDS filed June 15, 2004 have been considered. See attached documents.

Objection Withdrawn

4. The previous objection to the disclosure regarding listing the sequences without giving "SEQ ID NO:" is withdrawn in view of applicant's amendment to the specification in the amendment filed June 15, 2004.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

5. The previous rejection of claims 2, 4, 5, 7, 9-17 and 19, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicant's amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 17-19 of the amendment filed June 15, 2004.

Claim Rejections - 35 USC § 102

6. The previous rejection of claims 1-7, under 35 U.S.C. 102(b) as being anticipated by Stada *et al.* (Nucleic Acids Res. 22, 1394-1399 (1994)), is withdrawn in view of applicant's amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 19-21 of the amendment filed June 15, 2004.

7. The previous rejection of claims 1, 3, 6, 7, 11 and 12, under 35 U.S.C. 102(b) as being anticipated by Ganoza *et al.* (Proc. Natl. Acad. Sci. USA 82, 1648-1652 (1985)), is withdrawn in view of applicant's amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 21-22 of the amendment filed June 15, 2004.

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Objection to New Matter Added to Specification

8. The amendment filed June 15, 2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The original specification does not disclose adaptor nucleic acid in a composition for forming a polymer, and the new claims 45-51 recite the new matters.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

9. Claim 4 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 2. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

10. Claim 5 is objected to because of the use of the term "□-cyanoalanine". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 45-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 45-51 are directed to a composition for forming a polymer comprising a nucleic acid template, four or more adaptor nucleic acid species which base pairs to the nucleic acid template, and each adaptor nucleic acid species is physically coupled to a non-naturally occurring monomer, and a means for polymerizing the monomers into a polymer when the adaptor nucleic acid species are hybridized to the nucleic acid template. The specification only indicates the invention provides *in vitro* translation of an mRNA molecule with one or more tRNA molecules that are charged with naturally or non-naturally occurring amino acids or amino acid analogs, and the minimal translation system includes macromolecular components such as ribosomes, mRNA, aminoacyl tRNAs and translation factors; and a full length product has been synthesized using the four different unmodified tRNA^{Asn} variants chemically aminoacylated with mS (O-methylserine) for the T codon, and aG (allyglycine) for the N, S, V codons, (page 19, lines 25-34; page 28, line 32-page 29, line 5; Figs. 14 and 15; Table 5), however, the specification does not disclose a composition for forming a polymer, which the composition comprising four or more adaptor nucleic acid species, and where the adaptor nucleic acid species are not defined. Furthermore, there is no indication other polymers besides peptide or peptidomimetic product being synthesized using an *in vitro* translation system. The lack of description of a composition for forming a polymer, which the composition comprising a nucleic acid template, four or more adaptor nucleic acids, and a means for polymerizing the monomers into a polymer, applicants have failed to sufficiently describe the claimed invention, in such full,

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clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 8 and 44-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 8 recites the limitation "said inactive tRNA species" in lines 8. There is insufficient antecedent basis for this limitation in the claim.

14. Claims 45-51 are indefinite because of the use of the terms "adaptor nucleic acid" and "a means". The cited terms render the claim indefinite, it is not clear what "adaptor nucleic acid" is since the specification does not define the term, and what "a means" indicates. Claims 46-51 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 7, 19, 24 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Holsaka *et al.* (J. Am. Chem. Soc. 121, 12194-12195 (1999)).

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Hohsaka *et al.* disclose incorporation of two different non-natural amino acids into two different sites of a single protein by combining two four-base codons (page 12194, left column, paragraph 3). The mutated mRNA containing two four-base codons CGGG and AGGU, respectively, at Tyr54 and Thr57 sites of streptavidin, and the tRNAs containing the four-base anticodons and charged with respective non-natural amino acids (Lys(NBD) and 2-naphthylAla) were added into the *E. coli* in vitro protein synthesis system, where the translation product, full length streptavidin was synthesized and the double incorporation into streptavidin was confirmed by western blots and HPLC analysis (12194, right column; page 12195, right column; claims 7, 19, 24 and 39). Since the translation system utilizes two tRNAs containing the four-base anticodons and charged with respective non-natural amino acids for synthesizing mutated streptavidin, thus it lacks two active wild type elongator amino acyl tRNA; and the *E. coli* in vitro protein synthesis system is known to contain translation factors, which meet the criteria of claim 7. The recitation of “capable of translating exogenously added mRNA with highly selective incorporation at each codon” indicates the translation with high selectivity at each codon may or may not occur because of the term “capable of”, thus the limitation does not give weight to the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 11, 14, 23, 38, 40, 41 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Rothschild *et al.* (U. S. Patent 5,643,772, July1, 1997).

Rothschild *et al.* teach a preparation of nascent proteins translated in a cell-free translation system using non-radioactive markers which have electromagnetic spectral properties, where a non-radioactive marker is misaminoacylated to a tRNA molecule, and the misaminoacylated tRNA is added to the translation system and incubated to incorporate marker into the peptide (column 5, lines 10-40), where the nascent protein can be isolated (column 22, line 25-column 23, line 20; claim 38). Cell-free translation systems include *E. coli* lysates, or wheat germ extracts, and mixtures of purified translation factors or combination of lysates or lysates supplemented with purified translation factors (column 7, line 59-column 8, line 11; claim 23), and it is suggested to incorporate more than one marker into a single species of protein utilizing different tRNAs which are each misaminoacylated with different markers, e.g., coumarin amino acid used to misaminoacylate a tryptophan tRNA and a dansyllysine used to misaminoacylate a lysine tRNA (column 21, lines 58-67; Fig. 5; Examples 1-2; claims 1, 11; 44), where the aminoacyl tRNA is synthesized from a tRNA lacking a terminal CA dinucleotide (Fig.

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3; Example 2; claims 40, 41) Rothschild *et al.* also teach cell-free system may be coupled transcription/translation systems where DNA is introduced to the system, and transcribed into mRNA (column 8, lines 12-24; Example 3; claim 14). Although the examples of the patent only demonstrate one elongator tRNA charged with an amino acid analog (Examples 5 and 7), the reference does indicate that it may be advantageous to incorporate more than one marker into the protein because multiple misaminoacylated tRNAs can be used in the combined isolation and detection of nascent proteins, e.g., biotin-lysine marker could be used to misaminoacylate one tRNA and a coumarin amino acid marker could be used to misaminoacylate a different tRNA, magnetic particles coated with streptavidin which binds the incorporated lysine-biotin would be used to isolate nascent protein from the reaction mixture, and the coumarin marker could be used for detection and quantification (column 22, lines 25-33). Therefore, at the time of invention was made, it would have been obvious that one of ordinary skill in the art is motivated to use more than one tRNAs which are misaminoacylated with different markers in the translation system, which results in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made. The recitation of "capable of translating exogenously added mRNA with highly selective incorporation at each codon" indicates the translation with high selectivity at each codon may or may not occur because of the term "capable of", thus the limitation does not give weight to the claim.

Claim Objections

17. Claims 2, 6, 13, 15-17, 25-37, 42 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Conclusion

18. Claims 1, 4, 7, 8, 11, 14, 19, 23, 24, 38-41 and 44-51 are rejected, and claims 2, 5, 6, 13, 15-17, 25-37, 42 and 43 are objected. It appears claims 9 and 10 are free of art and allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. *CMK*

Patent Examiner

CMK

September 15, 2004

A handwritten signature in black ink, appearing to read 'Jon Weber', with a large, stylized initial 'J' and a long, sweeping horizontal stroke at the end.

JON WEBER
SUPERVISORY PATENT EXAMINER